IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

ZLOKOVIC et al.

Confirmation No. 1588

Atty. Ref.: 4061-32

Appln. No. 10/529,748

T.C. / Art Unit: 1649

Filed: March 30, 2005

Examiner: D.E. Kolker

FOR: PROTEIN S PROTECTS THE NERVOUS SYSTEM FROM INJURY

* * *

DECLARATION UNDER 37 CFR § 1.132

Berislav V. Zlokovic and John H. Griffin declare the following:

1. We are the original, first and joint inventors of the subject matter which is claimed in this application.

2. We have reviewed the claims pending in this application after entry of the claim amendments filed on April 15, 2008.

3. On information and belief, the Examiner cited as prior art under Section 102(a) the abstract of Cheng et al., which was published as Soc. Neurosci. Abstract 390.13 (see attached).

4. On information and belief, this application claims priority benefit of Application No. 60/414,333 filed September 30, 2002 and the earliest claimed priority date is less than one year after the publication of Cheng et al.

5. The authors of the abstract are T. Cheng, D. Liu, J. Fernandez, J.H. Griffin, and B.V. Zlokovic.

6. T. Cheng and D. Liu worked under and were supervised by Berislav V. Zlokovic.

7. On information and belief, neither T. Cheng nor D. Liu has asserted that he is an inventor of the subject matter which is claimed in this application.

8. J. Fernandez worked under and was supervised by John H. Griffin.

9. On information and belief, J. Fernandez has not asserted that he is an inventor of the subject matter which is claimed in this application.

10. The undersigned declare that all statements made herein of personal knowledge are true and that all statements made on information and belief are believed true; and further that these statements were made with the knowledge that any willful false statements are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of this patent application or any patent issuing thereon.

4/18/08
Date

Berislav V. Zlokovic

JENNIFER VOGEL
Printed Name of Witness

Witness' Signature

Date

John H. Griffin

Printed Name of Witness

Witness' Signature

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Date	Berislav V. Zlokovic
Printed Name of Witness	Witness' Signature
4/17/08 Date	John H. Griffin
DENICE MUNOZ Printed Name of Witness	Witness' Signature

7/9/1 (Item 1 from file: 5)
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NEUROPROTECTIVE AND ANTI - THROMBOTIC EFFECTS OF PROTEIN S IN A MURINE MODEL OF STROKE.
AUTHOR: Cheng T (Reprint); Liu D (Reprint); Fernandez J; Griffin J H; **Zlokovic B V** (Reprint
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ABSTRACT: **Protein S** is the anticoagulant protein in plasma and an important cofactor for activated protein C. Deficiencies in **protein S** are linked to the development of thrombosis and cerebral thrombophlebitis. **Protein S** is also a mitogen and exerts its cellular effects via the Axl tyrosine kinase receptor. In the present study, we examined the effects of **protein S** in a murine model of focal **ischemia** using middle cerebral artery occlusion/reperfusion technique. Mice (6 per group) received either purified human plasma-derived **protein S** or vehicle i.v. 10 min after stroke induction. **Protein S** reduced the infarction volume and brain edema in a dose-dependent manner, by 33% and 43% at 0.2 mg/kg, respectively, and by 57% and 62%, at 2 mg/kg, respectively. This correlated with significant improvement in the motor neurological score by 1.4-fold (0.2 mg/kg **protein S**) to 3.2-fold (0.5 and 2 mg/kg **protein S**). At 2 mg/kg, **protein S** reduced brain deposition of fibrin by 40% and improved the cerebral blood flow by 20-25% within the first hour of reperfusion. Intracerebral bleeding was not observed with **protein S**. Data indicate significant neuroprotective and anti-thrombotic effects of **protein S** in a murine model of stroke. We suggest that **protein S** should also be considered as a potential therapeutic agent for **ischemic** stroke in humans.